

REMARKS

Claims 11-15, 20-25, 32-37 and 39-73 are all the claims pending in this application. Claims 11-15, 20-25, 32-37, and 48-51 are withdrawn from consideration. Claims 39, 41, 42, 46, 52, 53 and 64 are currently amended. Applicants acknowledge the Office's acknowledgment of a claims for foreign priority under 35 U.S.C. § 119 (a)-(d) or (f).

Reconsideration of this application and allowance of the claims are respectfully requested in view of the following remarks.

Claim Rejections Under 37 C.F.R. §103

Claims 39-47 and 52-73 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Armitage *et al.* (WO 9220334) in view of Gregory *et al.* (U.S. Patent No. 5,262,179). The Examiner argues that Armitage discloses a pharmaceutical composition comprising ibuprofen salt in a racemic mixture of S-ibuprofen, such as alkaline earth metal salts, a carrier, a compressible filler component such as lactose, microcrystalline, and calcium phosphate combined with a disintegrating component such as maize starch and lubricating agents. The Examiner further argues that Armitage discloses the effective amounts of ingredients therein, such as a solid composition comprising a 10-99% of ibuprofen, 1-90% of a filler or diluent, 0.1-10% of a lubricating agent and other ingredients. Finally, the Examiner argues that Armitage discloses that the ibuprofen pharmaceutical composition tablets are coated with enteric coatings and hydroxypropylmethyl cellulose or polysaccharide is employed. However, the Examiner admits that the cited prior art does not expressly disclose the employment of the particular sodium carbonate or sodium bicarbonate 3-20% by weight in the ibuprofen dosage of Armitage and the particular amount of sodium salt of ibuprofen may be 40-60%.

Gregory, according to the Examiner, discloses ibuprofen salts have an unpleasant taste and it is advantageous to provide a dosage form that masks the taste of ibuprofen by incorporating an alkali metal bicarbonate into the dosage form, especially sodium bicarbonate. Therefore, the Examiner concludes that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular sodium carbonate or

sodium bicarbonate in 3-20% by weight in the ibuprofen dosage of Armitage and the amount of sodium salt of ibuprofen may be 40-60% in the compositions of the prior art cited. One of ordinary skill in the art would have been motivated to employ the particular sodium carbonate or sodium bicarbonate 3-20% by weight in the ibuprofen dosage of Armitage because it is known that ibuprofen salts have an unpleasant taste and, therefore, it is advantageous to provide a dosage form that masks the taste of ibuprofen by incorporating an alkali metal bicarbonate into the dosage form, especially sodium bicarbonate according to Gregory.

Applicant respectfully disagrees that claims 39-47 and 52-73, as amended, are unpatentable over Armitage in view of Gregory. Armitage relates to a pharmaceutical composition that includes a specific enantiometric form of ibuprofen, namely S(-)-sodium ibuprofen (page 2, paragraph 4). The reasons and advantages for using this specific enantiomer are discussed at page 2, final paragraph to page 3, final paragraph. But Armitage does not relate to nor does it suggest the pharmaceutical compositions comprising the sodium salt of racemic ibuprofen as claimed in the present invention.

The Examiner refers to page 1, lines 8 to 22 as disclosure for a pharmaceutical composition comprising ibuprofen salt in racemic mixture of S-ibuprofen. However, this paragraph represents a discussion of the prior art. It does not mean Armitage embraces racemic forms of ibuprofen. In fact, quite the contrary, Armitage aims to overcome the problems associated with such a racemic mixture. Furthermore, nowhere does Armitage disclose a non-effervescent compressed dosage form including sodium carbonate, let alone that the inclusion of sodium carbonate provides the advantages of improved compressibility and disintegration characteristics. Thus, the disclosure of Armitage fails to disclose at least two essential features of the invention as claimed and teaches away from the claimed feature of the sodium salt of racemic ibuprofen.

Gregory relates to taste masking water soluble ibuprofen salts in aqueous solution. This is achieved by the inclusion of sodium bicarbonate, potassium bicarbonate and the corresponding monohydrogen phosphates and tribasic citrate salts (col. 2, line 62 to col. 3, line 4). Gregory

explicitly teaches away from the use of alkali metal carbonates as the resulting solution has an unacceptably high pH for oral administration (col. 3, lines 39 to 42). Consequently, a person of ordinary skill in the art upon reading Armitage and Gregory would not be motivated to produce a non-effervescent compressed dosage form comprising the sodium salt of racemic ibuprofen and sodium carbonate, as Armitage relates to the S(-) enantiomer of ibuprofen and Gregory teaches that sodium carbonate should not be included in ibuprofen salt formulations. There is no teaching or even a hint that would allow a person of ordinary skill in the art to achieve the present invention. Applicant respectfully requests that the rejection on this basis be withdrawn.

Claims 39-47 and 52-53 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Geyer et al. (U.S. 5,380,535) in view of Gregory for reasons of record. The Examiner further argues that one of ordinary skill in the art would expect a composition containing the same components to exhibit similar properties. Additionally, it is considered within the skill in the art to select optimal parameters in order to obtain beneficial effects. The recitation of the compression force leads the claim to a product-by-process claims. The Examiner is of the opinion that the prior art teaches dosage forms containing the same components as instantly claimed. Therefore, absent evidence of unexpected results, the crushing strength, disintegration time and compression force are not considered critical to the invention. The Examiner also argues that one having ordinary skill in the art would have been motivated to employ the particular sodium carbonate or sodium bicarbonate 3-20% by weight in the ibuprofen dosage of Geyer because it is known that ibuprofen salts have an unpleasant taste and, therefore, it is advantageous to provide a dosage form that masks the taste of ibuprofen by incorporating an alkali metal bicarbonate into the dosage form according to Gregory.

Geyer relates to chewable ibuprofen compositions which disintegrate rapidly in the mouth (col. 2, lines 24 to 26). The compositions may include a buffering agent such as sodium bicarbonate to reduce the burn effect associated with ibuprofen (col. 6, lines 16 to 24). Nowhere does Geyer disclose a pharmaceutical composition which includes sodium carbonate, let alone that the inclusion of sodium carbonate would provide the advantages of improved

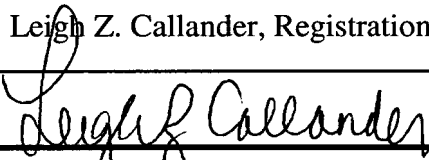
compressibility and disintegration characteristics.

The comments with respect to Gregory above apply equally here. The present application provides an improved compressed dosage form which is swallowed whole and permits delivery of high therapeutic levels of the sodium salt of racemic ibuprofen to the gastrointestinal tract of a patient. As stated in the present application at page 7, the sodium salt of racemic ibuprofen is a flaky, soft and sticky material. Consequently, it does not lend itself to formulation into a directly compressed dosage form as it typically sticks to the tableting punches. Moreover, it is also difficult to pre-granulate the sodium salt prior to compression with other excipients. In order to form satisfactory compressed dosage forms of the sodium salt of racemic ibuprofen it is necessary to pre-treat the salt, i.e. milling, etc. Unexpectedly, the inclusion of sodium carbonate in the carrier material permits the formation of a satisfactory compressed dosage form of the sodium salt of racemic ibuprofen without the need to initially pre-treat the ibuprofen. Conveniently, it is therefore possible to use sodium ibuprofen taken directly from a bulk production process, thereby significantly reducing the overall production costs (see page 7, lines 28 to 31 and page 2, lines 12 to 14).

It is inconceivable that a person of ordinary skill in the art would produce a non-effervescent compressed dosage form comprising the sodium salt of racemic ibuprofen and sodium carbonate. Furthermore, claims 39-47, 52, and 53 require the dosage form or formulation to be coated. Such coated dosage forms or formulations are swallowed as a whole, as defined in the claims. Thus, there is no disintegration or dissolution of the coated dosage form in the oral environment when swallowed as a whole and therefore no dispersion of the active ingredient in the aqueous environment of the human mouth. This is in contrast to the Examiner's assertions. Therefore, no taste masking is required or contemplated for such a coated dosage form or formulation as in claims 39-47, 52, and 53, as amended. For this reason there is no motivation to combine the teaching in Armitage with Gregory, where Gregory teaches including sodium bicarbonate as a taste masking component in a dosage form comprising sodium ibuprofen as the active ingredient. In light of the above, Applicant respectfully submits that a skilled person would

not even consider Geyer or Gregory, let alone combine the teaching of these references, in an attempt to provide a compressed solid dosage form adapted to be swallowed whole, as the taste masking issues discussed in Geyer and Gregory are not applicable to coated dosage forms that are swallowed. Therefore, Applicant submits that claims 39-47, 52, and 53 are not obvious over Armitage in view of Gregory and request that the rejection on this basis be withdrawn.

In view of the above remarks, Applicant submits that the present application is in condition for allowance. Reconsideration and favorable action are requested. The Examiner is invited to telephone the undersigned to expedite allowance of this application.

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